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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112701-818	3290

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
05/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,256	MOODYCLIFFE ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 15, 2010 has been entered.

Status of Claims

Claims 6-7 are pending and under examination on the merits in the instant case.

Claim Objections

Claim 6 is objected to because of the following informalities: Claim 6 is currently amended to recite "A composition for treating epithelial tissue damage" as applicant has deleted the phrase "preventing or" in line 1. However, the claim still recites "a substance that prevents or treats epithelial tissue damage" in lines 2-3. It appears that the phrase "prevents or" in line 3 should be deleted for consistency of claim language. Appropriate correction is required.

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 7 depends from claim 6. Claim 6 as written claims that the "RNA polynucleotide" is "antisense to a sequence comprised by the glucosylceramide synthase mRNA". See lines 4-5. Hence, the RNA polynucleotide

claimed in claim 6 is inherently equivalent to a complementary RNA to glucosylceramide synthase mRNA. As such, the mere recitation that "the polynucleotide is a cRNA" in claim 7 does not further limit the subject matter of claim 6 because the "antisense" RNA of claim 6 or the "complementary" RNA of claim 7 is structurally and functionally equivalent and interchangeable, absent evidence to the contrary. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims recite limitations that are not adequately supported by the application as originally filed. The composition of claims 6-7 requires two elements: an RNA antisense to glucosylceramide synthase mRNA and a cell containing both the RNA antisense and a lower amount of the CD1d gene translation product. However, there does not appear to be a written description for the claimed limitation "an RNA polynucleotide antisense to a sequence

comprised by the glucosylceramide synthase mRNA, and further comprising a cell containing the polynucleotide and a lower amount of the CD1d gene translation product than in similar cells lacking the polynucleotide." in the application as originally filed. Accordingly, the claimed limitation is considered to introduce new matter which is not adequately described in the application as originally filed.

Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered when analyzing claims for compliance with the written description requirement include: A) actual reduction to practice; B) disclosure of drawings or structural chemical formulas; C) sufficient relevant identifying characteristics (e.g., complete structure, partial structure, physical and/or chemical properties, structure/function correlation); D) method of making the claimed invention; E) level of skill and knowledge in the art; and F) predictability in the art.

In the instant case, claims 6-7 are drawn to a composition comprising a cell that contains an antisense RNA that is complementary to glucosylceramide synthase (GCS) mRNA, wherein the cell that contains the antisense RNA has a reduced amount of CD1d gene product compared to the cell that does not contain the antisense RNA, wherein the composition is intended to treat or prevent epithelial tissue damage.

With regard to the claimed composition, the instant specification makes it clear that the inventors did not reduce the claimed composition to actual practice as evidenced by the complete lack and absence of the claimed composition that is actually synthesized or shown to have a potential to treat or prevent any and all epithelial tissue damages.

In addition, there is no structure/function correlation for the antisense (or complementary) RNA that is complementary to GCS mRNA. That is, neither the specification nor the state of the art taught that such antisense (or complementary) RNA is capable of reducing CD1d gene product in a cell, let alone its therapeutic ability to treat epithelial tissue damage. Again, as repeatedly pointed out in previous Office actions as well as hereinabove, the instant specification is completely silent about the "actual" demonstration of the functional roles of antisense (or complementary) GCS RNA. In addition, it was known in the art that GCS inhibition in a cell results in the up-regulation of CD1d in cells. See for example Sriram et al. (*PNAS,* 2002, 99:8197-8202), who teach that an GCS inhibitor, PPMP, up-regulates CD1d1 in T cell lymphoma cells. See page 8200, left column: "Treatment of L5178Y-R cells with PPMP could potentially influence CD1d1 function via the up-regulation of this cell surface antigen." Consistent with the experimental observation of Sriram et al., it was later discovered by a different group of researchers that reduced activity of glucosylceramide (synthesized by GCS) results in the increased expression level of CD1d. See Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676, citation of record). Hence, the opposite biological effect (i.e., increased expression level of CD1d) to the claimed biological effect (i.e., reduced or lower amount of the CD1d gene translation product) was known to be the consequence of GSC reduction. As such, the knowledge and skill pertaining to making a composition comprising an antisense RNA targeted to GSC and a cell having the antisense RNA and a lower amount of

CD1d compared to cells not having the antisense RNA were not available in the art at the time the invention was made. Furthermore, neither the instant specification nor the state of the prior art teaches that the composition is "a substance that prevents or treats epithelial tissue damage" as claimed, and therefore, one would not have predicted, based on the disclosure of the instant specification and the teachings of Sriram et al., that the composition would indeed contain a cell having a lower amount of CD1d due to the antisense RNA, let alone the therapeutic utility of the composition for treating epithelial tissue damage as claimed.

In addition, the claimed "epithelial tissue damage" is so broad and generic that it encompasses any type of damage (e.g., burns, cuts, inflammation, scars, bruises, tumor formation) of any type of epithelial tissue (e.g., kidney epithelial tissue, lung epithelial tissue, any organ having an epithelial tissue). Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). See also MPEP §2163.

In the instant case, the specification is completely silent about which specific epithelial damage is treated or prevented with the claimed composition. That is, there is not a single disclosed species within the claimed genus of epithelial tissue damages claimed to be treated or prevented.

In light of the above, the instant specification does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention. Further, the specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the genus claimed in the instant case.

Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction

provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claimed composition requires that the anti-glucosylceramide synthase (GCS) antisense polynucleotide treatment result in a concurrent reduction in the amount of CD1d in a cell. However, neither the specification nor the state of the prior art establishes the required relationship between reduced GCS and reduced CD1d. In fact, contrary to the claimed relationship between reduced GCS and reduced CD1d, it was known in the art that GCS inhibition in a cell results in the up-regulation of CD1d in cells. See for example Sriram et al. (*PNAS,* 2002, 99:8197-8202), who teach that an GCS inhibitor, PPMP, up-regulates CD1d1 in T cell lymphoma cells. See page 8200, left column: "Treatment of L5178Y-R cells with PPMP could potentially influence CD1d function via the up-regulation of this cell surface antigen." Further, the teachings of Sriram et al. are further verified by a post-filing reference. See Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676, citation of record), who teach that reduced activity of glucosylceramide, which is synthesized by glucosylceramide synthase, results in the increased expression level of CD1d. Hence, it is reasonable to expect that an antisense polynucleotide against GCS would increase, not decrease, the amount of CD1d in a cell, which is the opposite effect of the claimed composition. Again, the instant specification fails to show the necessary nexus between reduced glucosylceramide synthase mRNA expression and the required reduction in CD1d and the therapeutic utility for epithelial tissue damage treatment and prevention as claimed in the instant case. Instead, the specification merely provides a hypothetical, unproven theory that one can block the function of CD1d by reducing GCS mRNA.

See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004): "Nascent technology, however, must be enabled with a specific and useful

teaching. The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." (emphasis added).

In view of the foregoing, the quantity of experimentation needed to make and use the invention based on the content of the disclosure would be undue, because the enabling disclosure is not commensurate in scope with the claimed therapeutic composition. Since the issues described above are not satisfactorily resolved herein, it is concluded, based on the evidence as a whole, that the instant specification fails to teach how to make and use the claimed invention without undue experimentation.

Response to Arguments

Applicant's arguments filed on February 15, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are fully enabled because the specification "discloses a relationship between CD1d expression and skin irritation/inflammation." by pointing out pages 5 and 9 of the specification. First, applicant's attention is directed to the fact that the claims are not specifically directed to an anti-CD1d composition for treating "skin irritation/inflammation". As noted hereinabove, the claims are broadly drawn to a composition for treating or preventing any and all types of "epithelial tissue damage". Further, as extremely evident from the claim language, the claimed composition does not comprise an anti-CD1d compound; it comprises an antisense RNA complementary to GCS and a cell containing the antisense RNA as well as a lower amount of CD1d. It is found that neither page 5 nor page 9

"discloses" or establishes the required cause-and-effect relationship between anti-GCS antisense RNA (cause) and lower amount of CD1d (effect), which is intended to be used to treat or prevent any and all types of epithelial tissue damage including but not limited to skin irritation and inflammation. It is noted that page 5 prophetically describes that blocking CD1d may be useful for treating skin or epithelial cell damage and page 9 describes that "apart from the CD1d gene being the target", "ceramides and/or glucosylceramides, may be modified such, that they exert the desired effect on the CD1d molecule." There is nothing whatsoever in the passages pointed out by applicant that clearly establishes the required nexus between anti-GCS antisense RNA and reduction of CD1d with requisite epithelial tissue damage treatment effects. Page 9 (WO 2004/019900) is the only place that mentions the instantly claimed target gene "glucosylceramide synthase" such that "the number of the glucosylceramide synthase transcripts may be reduced by designing an polynucleotide antisense to at least a part of the glucosylceramide synthase gene or glucosylceramide synthase mRNA, so that eventually the signal to epithelial cells to proliferate is turned down. The nucleotide sequence of the glucosylceramide synthase gene is disclosed in Ichikawa et al." This disclosure pertaining to glucosylceramide synthase does not whatsoever demonstrate or teach or suggest that reducing GCS lowers CD1d, let alone treat or prevent any type of epithelial tissue damage as broadly claimed in the instant case. Hence, contrary to applicant's allegation that a person of ordinary skill in the art "would therefore understand that reducing the amount of glucosylceramide synthase blocks or modifies the activity of the CD1d molecule and can be used to treat or prevent tissue damage.", the instant specification does not provide sufficient guidance/information on the necessary link between anti-GCS antisense and CD1d reduction/epithelial tissue damage treatment or prevention.

Applicant argues that the claims are fully enabled because the state of the art was sufficiently developed to enable one to make the claimed invention by pointing out Deng et al. (2002) and Struckhoff et al. (2004). First, applicant's attention is directed to the fact that applicant has not properly submitted and recorded the cited references in a proper format (e.g., IDS). Second, applicant's attention again directed to the fact that the crux of the instant enablement rejection is the lack of the nexus between an anti-GCS antisense and CD1d reduction, which is the claimed, required structure/function correlation. It is found that neither the Deng et al. reference nor the Struckhoff et al. reference teaches the claimed structure/function correlation as either of the references does not teach that anti-GCS antisense reduces CD1d and that a composition comprising a cell having both the antisense GCS antisense and a lower amount of CD1d treats or prevents any and all kinds of epithelial tissue damage. Hence, neither Deng et al. nor Struckhoff et al. provided "evidence that the specification as filed enabled one of skill in the art to make and use the disclosed invention". Third, applicant's attention is directed to the fact that the Deng et al. reference applicant has relied on in support of applicant's argument is the prior art reference used to reject claims 1, 3, and 6-7 under 35 U.S.C. 102(a), wherein the previous claims were merely drawn to an anti-GCS antisense composition for treating epithelial tissue damage and did not require the instantly claimed association between GCS reduction and CD1d reduction. See page 5 or the Office action dated February 23, 2009. Hence, examiner is well aware of the state of the prior art pertaining to making and using an anti-GCS antisense molecule for melanoma treatment as taught by Deng et al. Nevertheless, as noted hereinabove, Deng et al. do not teach the claimed feature: "a cell containing the polynucleotide and a lower amount of the CD1d gene translation product than in similar cells lacking the polynucleotide.", and nor does the instant specification teach the aforementioned claimed feature.

Since applicant's arguments are not persuasive at all for the reasons stated hereinabove, this rejection is reapplied in the instant Office action.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi (Acting SPE) can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
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